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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/572,732	07/18/2006	Kurt R. Zinn	21085.0050U2	5282

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EXAMINER	
KELLY, ROBERT M	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
01/27/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,732	ZINN ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *124,126,127,163,164 and 166-175* is/are pending in the application.

4a) Of the above claim(s) *126 and 127* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *124,163,164 and 166-175* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *In re Alonso 88 USPQ.2d 1849 (Fed Cir 2008)*

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/18/10 has been entered.

Claim 124 is amended.

Claims 124, 126, 127, 163, 164 and 166-175 remain pending.

Election/Restrictions

It is noted that the presently pending claims all fall with the elected invention: that of Group VI, methods of treating inflammation by administration of a complement modulator, as elected in the election of 11/20/08. Moreover, the invention is considered with respect to the elected species, SEQ ID NO: 9, and Claims 126 and 127 remain withdrawn.

Claims 124, 126, 127, 163, 164, and 166-175 are considered with respect to SEQ ID NO: 9.

Specification

TITLE

The objection to the title is withdrawn, as Applicant's amendment now refers to reducing complement activation.

Claim Objections

In light of the amendment to Claim 124, the objections to Claims 124, 126, 127, 163, 164, and 166-175 are withdrawn.

To wit, the amendment now recites that the complement modulator is displayed on the surface of the vector.

Claim Rejections - 35 USC § 112 - clarity

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In light of the amendments, the rejections of Claims 124, 126, 127, 163, 164, and 166-175 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, are withdrawn.

To wit, the claims have been amended to recite that the complement modulator is displayed on the surface, and the method is performed during gene therapy.

Claims 124, 163, 164, and 166-175 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 124 recites, in the preamble, that the method is for reducing complement activation during gene therapy in a subject. However, there is no commensurate conclusion indicating that

complement activation is reduced during the therapy, and hence, the Artisan would not be reasonably informed of the metes and bounds of the claims. To wit, is more required of the claim to infringe, perhaps from the specification?

Claims 163, 164, and 166-75 are rejected for depending from a rejected base claim(s) and not overcoming the lack of clarity therein.

Claim Rejections - 35 USC § 112 – new matter, in gene therapy

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 124, 163, 164, and 166-175 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for specifically encompassing NEW MATTER. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 124, given its broadest reasonable interpretation, appears to indicate that inflammation is reduced in any gene therapy protocol, by the claimed method, administered separately, as a separate vector (i.e., the vector which induces inflammation is not the vector delivering the gene in the gene therapy). Such is determined to be specifically encompassed because the vector itself is not required to carry a transgene for any form of therapy, and the method appears to indicate that complement is inhibited simply by the vector, yet the claim specifically states "during gene therapy".

The depending claims are rejected for depending from the base claim and not overcoming the broad generic interpretation specifically encompassed.

Applicant's specification indicates that the vector itself is meant of the gene therapy protocols, as a proclaimed-new vector for use in gene therapy (e.g., paragraph 0116 and 0118 of the Application Publication, as stated by Applicant's response).

However, given the only statements are to utilize it as the vector for affecting gene therapy, the Artisan would not have understood Applicant to have been in possession of the specifically encompassed secondary-to-gene therapy treatment, to reduce inflammation.

Therefore, the claims are properly rejected for comprising new matter.

Response to Argument – *New Matter, "in gene therapy"*

Applicant's response of 11/18/10 has been fully considered but is not found persuasive.

Applicant argues that the Examiner has failed to meet the office burden to articulate a reasonable basis challenging the adequacy of the written description with findings of fact (p. 8, paragraph 3).

Such is not persuasive. Citations are provided from the specification, and a finding of no support for separate administration of the vector from the gene therapy vector administered during the gene therapy. These are findings of fact, and support the rejection. It should further be noted that a single species being provided does not provide adequate written description for a genera (In re Alonso, 88 USPQ.2d 1849 (Fed Cir 2008)). Applicant's specification only supports the species of the gene therapy vector being the vector displaying the complement modulator on its surface, and hence, fails to provide adequate description for the genera of any administration "during gene therapy".

Applicant cites several paragraphs from the Specification, via the Application Publication, 2007/0036721, to argue that possession of viral vectors for use in gene therapy, paragraphs 0113, 0116, 0121, 0123, 0124, 0275, and 0302. These are argued to say, specifically (i) inhibition of complement activation has the added benefit of decreasing the humoral and cell mediated immune response to virus, (ii) inhibition of complement can be used to reduce redirection of the vector, thereby allowing its concentration in a desired location, (iii), innate and systemic immunity can be considered in the design of the vector, (iv) two general strategies exist for the reduction of immune activation that accompany viral vector delivery, and (v) the vectors disclosed can decrease these effects for gene therapy vectors. (pp. 8-9, paragraph bridging.)

Such is not persuasive. The question is whether or not the Artisan would have considered Applicant to have been in possession of the invention as claimed at the time of filing. Simple quotes out of context can be misleading, and hence, each must be individually addressed herein. First, the quote (i) above, from paragraph 0275 of the Application publication, is discussing complement activation works to provide two benefits, but is limited to the adenoviral vector, which displays the modulator, which in context of the whole paragraph, is that complement inhibition can be a valid approach to overcome the liver's propensity to remove adenoviral vector designed to target other tissues and organs. Hence, this quote is from a paragraph clearly limited to inhibition of complement activation against the same vector, which is an adenoviral vector. While from this information, one may provide some enablement for the Artisan who wishes the vector to be separate from the vector which provides the gene therapy, such is insufficient for a clear demonstration of possession. Quote (ii) above, from paragraph 0113 of the same publication, clearly in the quote itself indicates that redirection of the vector itself is what is of

concern, and if the vector for the gene therapy is what is of concern, the redirection of the secondary vector is not of concern. Quote (iii) above, from paragraph 0120 of the same publication, indicates simply that both immunities can be considered, however, even within the whole paragraph, gives no indication that it should be used for the inhibition of complement against other vectors. Quote (iv) above, from paragraph 0120 of the same publication, appears to indicate that two strategies exist, which, it appears Applicant wishes to imply that the two strategies are that the gene therapy vector can carry the modulator, or, alternatively, that a second vector can carry the modulator. However, as given in context of the whole paragraph, and the subsequent paragraphs (paragraphs 0121-0124), indicate that the first strategy is one of displaying a factor that binds to the factors that are negative regulators of complement, or result in functional inhibition (in paragraph 0120); and the second strategy being to encode and display negative regulators of complement directly (in paragraph 0124). Hence, this quote has nothing to do with the argument. Quote (v) above, from paragraph 0116 of the same publication, is perhaps Applicant's strongest argument in that the literal wording is one of "can decrease these effects for gene therapy vectors", however, it simply is not clear enough that the vectors are meant to encompass separate vectors administered during gene therapy with another vector. It could be just as easily interpreted to mean that the vectors used in the specification exhibit reduced complement activation effects when used as gene therapy vectors. Moreover, given no further disclosure of separate vectors, the Artisan would not reasonably conclude Applicant had possession of the invention as claimed.

Applicant argues that they are precisely claiming separate administration of the vector, and that complement is modulated by the displayed modulator, and that gene therapy is not

required for complement inhibition, and reference gene therapy is simply a reference to one use, which is admitted by the Examiner (p. 9, paragraph 2).

Such is not persuasive. The evidence may support enablement, in that the vector may inhibit complement against other vectors coadministered, but Applicant has in fact limited it to a gene therapy protocol in which the administration takes place, and the specification only provides such description to the vector which is the gene therapy vector which is to display the modulator. As such, Applicant has not sufficiently described, at the time of invention, use of these vectors in gene therapy, without the vector being same as the one which performs gene therapy. Applicant's argument goes more toward enablement than the blaze marks which indicate possession of the invention at the time of filing.

Claim Rejections - 35 USC § 112 – New Matter, gene of interest

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of further consideration, the rejections of Claims 124, 163, 164, and 166-175 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for claiming or specifically encompassing new matter, are withdrawn.

The claims are found to be possessed for gene of interest, given the broad description throughout the specification. The limitation of gene of interest to reporters is considered to be more of antecedent basis rather than a demonstration of possession, and is not limiting.

Claim Rejections - 35 USC § 112 – new matter, targeting motifs

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 124, 163, 164, and 166-175 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for claiming or specifically encompassing new matter, for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 171 requires the viral vector to comprise a targeting motif. The other claims are parent to, depend from 171, or depend separately from the same parent claim, Claim 124, and hence, specifically encompass such.

Applicant cites paragraph 140 (sic) for support. It is assumed that Applicant meant to recite paragraph 104. However, 104 is limited to adenoviral vectors with targeting motifs.

Still further, the specific motifs are supported by the same averred paragraph, as well paragraphs 105-108. It is noted however, the same paragraphs are also limited to adenoviral vectors.

Lastly, it should be noted that the original claims do not provide any support for targeting motifs.

Hence, the Artisan would not have understood Applicant to have been in possession of the invention as claimed, for the generic viral vectors encompassed.

Therefore, the claims are properly rejected for claiming or encompassing specifically, the invention as claimed.

Response to Argument – *New Matter, "targeting motif[s]"*

Applicant's response of 11/18/10 has been fully considered but is not found persuasive.

Applicant argues no finding of fact was provided and reasonable basis therefrom, to support the rejection (p. 11, paragraph 4).

Such is not persuasive. There were findings of fact, as given in the rejection, and such facts were shown to not support possession of the generic embodiment claimed. The Examiner suggests that Applicant fully explain what is meant by the accusation. Why are the facts and reasoning provided not findings of fact, and reasoned basis, respectively?

Applicant quotes paragraph 0102 of the specification of the Publication, to argue that many vector types are taught, and hence, possession is found (pp. 11-12, paragraph bridging).

Such is not persuasive. There is no rejection for a generic vector, the rejection is for a generic vector comprising a targeting motif. There is no description for a targeting motif being used in a generic vector, but only one species: adenoviral vectors. A single embodiment does not provide support for a broad genera (In re Alonso, 88 USPQ.2d 1849 (Fed Cir 2008)).

Applicant argues that the prior Art was capable of performing such, and it was known in the prior Art to utilize targeting motifs (p. 2, paragraph 2).

Such is not persuasive. This is an amended claim, which requires support from the specification to demonstrate possession at the time of filng, and providing support from the prior art amounts to obviousness-type support, which is not a basis for possession. Applicant's argument may support enablement, but not possession. Applicant's argument to local delivery

and efficiency/safety is not understood, and seems to have little to do with the rejection, so it is not further addressed herein.

Claim Rejections - 35 USC § 112 – limitations of claim 175

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

While the rejections on the basis of a promoter are withdrawn: Claims 124, 163, 164, and 166-175 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for specifically claiming or encompassing new matter, for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 175 is drawn to generic CAR binding site mutants or ablation of integrin binding, to a generic viral vector.

The balance of the claims are generic as being the parent claim or separately-depending from the parent claim.

Applicant cites paragraph 118 to support the CAR binding site mutants, as well as ablation of integrin binding. However, such paragraph is similarly limited to adenovirus.

Moreover, the claims are amended, and are required to demonstrate support from the specification for possession, and use of art therefore would require an obviousness-type support, which is insufficient to demonstrate possesion.

Hence, the Artisan would not have understood Applicant to have been in possession of the generic invention claimed at the time of invention.

Therefore, the claims are properly rejected for claiming or specifically encompassing new matter.

Response to Argument – New Matter, claims 173 and 175

Applicant's response of 11/18/10 has been fully considered but is not found persuasive.

Applicant argues a failure to provide a reasonable basis, supported with findings of fact (p. 13, paragraph 2).

Such is not persuasive. The Examiner has stated several facts, and shown how they are reasoned to show a lack of possession at the time of filing.

Applicant argues possession of a promoter, citing paragraph 0089 for a definition of the promoter, and paragraph 0110 for an example, and paragraph 0018 for support of a reporter operably linked to the promoter (p. 13, paragraph 4).

Such is not persuasive. The rejection is not a rejection for a generic lack of support of a promoter. The rejection is for a generic vector with ablated integrin binding or a mutation to CAR binding site. The information regarding the promoter is because such was cited by Applicant for support. Specifically, Applicant cited paragraphs 108-109 which appear to have nothing to do with integrin binding ablation or CAR binding mutant. The balance of the Argument in this paragraph is not addressed, as the rejection is for the subject matter of Claims 173 and 175, which are not limited to adenoviral vectors, and therefore, also is specifically embraced by the broad claims (parent claims and separately depending claims).

Applicant argues that the prior Art was aware of CAR binding mutants, for coxsackievirus and adenovirus, and integrin-binding and its ablation, and the importance of all of these (pp. 13-14, paragraph bridging).

Such is not persuasive. First, it should be noted that Applicant's claims are amended claims, and therefore, reliance on Art to demonstrate possession is then one of obviousness-type possession, and such is insufficient to demonstrate possession. Second, with regard to the CAR binding mutants, Applicant states that there are "at least two viruses, e.g., coxsackievirus and adenovirus", however, it is a fact that there are only two: cosackievirus and adenovirus. Third, a single embodiment (adenovirus) does not provide possession of a genera (Applicant's argued "at least two") (In re Alonso, 88 USPQ.2d 1849 (Fed Cir 2008)). Fourth, at no point does Applicant recognize in the specification that coxsackievirus is one virus which may be mutated in CAR-binding, nor does Applicant at any point in the specification provide any other embodiment for integrin ablation, except that of adenovirus. Possession of a single embodiment (adenovirus) fails to provide adequate support for a genera (In re Alonso, 88 USPQ.2d 1849 (Fed Cir 2008)). Applicant's arguments go toward helping with enablement, but fail to meet the bar for possession of an amended claim at the time of filing.

I. Base Rejection: retroviral vectors with a generic complement inhibitor on its surface and encoded by the genome. This demonstrates the non-allowability of the broad claim as compared to the various species.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of the amendments, the rejections of Claims 124, 170, 171, and 173 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,643,770 to Mason, et al., are withdrawn.

To wit, Mason teaches placing of the complement-inhibitor-coded sequence in trans, and therefore, the virus does not encode such sequence.

II. Modifications of the Retroviral Base Rejection to Utilize Adenoviral Vectors

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

In light of the amendments, the rejections of Claims 124, 163, and 170-173 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., are withdrawn.

To wit, as shown above, the 102 base reference, Mason, does not teach the feature of encoding the complement-inhibiting sequence.

III. Modification of (II) to Utilize a Hypervariable Region

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

In light of the amendments, the rejections of Claims 124, 163, and 170-173 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., as applied to claims 124, 163, and 170-173 above, and further in view of U.S. Patent No. 6,127,525 to Crystal, et al., are withdrawn.

To wit, as shown above, the 102 base reference, Mason, does not teach the feature of encoding the complement-inhibiting sequence.

IV. Modification of (II) or (III) to utilize ED1

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

In light of the amendments, the rejections of Claims 124, 163, and 169-173 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al as applied to claims 124, 163, and 170-173 above (II), and further in view of Inal, et al. (2000) FEBS Letters, 470: 131-34, are withdrawn; and

The rejections of Claims 124, 163, and 169-173 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., and U.S. Patent No. 6,127,525 to Crystal, et al., as applied to claims 124, 163, and 170-173 above (III), and further in view of Inal, et al. (2000) FEBS Letters, 470: 131-34, are withdrawn.

To wit, as shown above, the 102 base reference, Mason, does not teach the feature of encoding the complement-inhibiting sequence.

V. Modification of (IV) to Further Include a His-Tag

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

In light of the amendments, the rejections of Claims 124, 163, 167, and 169-174 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., and Inal, et al.

(2000) FEBS Letters, 470: 131-34 as applied to claims 124, 163, and 169-173 above (II), and further in view of Huang, et al. (2000) Protein Expression and Purification, 18: 169-74, are withdrawn; and

The rejections of Claims 124, 163, 167, and 169-174 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., U.S. Patent No. 6,127,525 to Crystal, et al., and Inal, et al. (2000) FEBS Letters, 470: 131-34 as applied to claims 124, 163, and 169-173, and further in view of Huang, et al. (2000) Protein Expression and Purification, 18: 169-74, are withdrawn.

To wit, as shown above, the 102 base reference, Mason, does not teach the feature of encoding the complement-inhibiting sequence.

VI. Modification of V to Utilize 2 ED1 Sequences and a Linker

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

It is noted that the following rejections rely upon Oh, et al., which is a reference under 102(a), and hence, may be sworn behind to overcome the rejection.

In light of the amendments, the rejections of Claims 124, 163, 166, 167, and 169-174 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al.,

Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., Inal, et al. (2000) FEBS Letters, 470: 131-34, and Huang, et al. (2000) Protein Expression and Purification, 18: 169-74 as applied to claims 124124, 163, 167, and 169-174 above, and further in view of Oh, et al., (2003) Immunology, 110: 73-79, are withdrawn; and

The rejections of Claims 124, 163, 166, 167, and 169-174 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., U.S. Patent No. 6,127,525 to Crystal, et al., Inal, et al. (2000) FEBS Letters, 470: 131-34, and Huang, et al. (2000) Protein Expression and Purification, 18: 169-74 as applied to claims 124, 163, 167, and 169-174, and further in view of Oh, et al., (2003) Immunology, 110: 73-79, are withdrawn.

To wit, as shown above, the 102 base reference, Mason, does not teach the feature of encoding the complement-inhibiting sequence.

VI. Modification of (II) to Utilize an AAV vector (AAV vector in AdV envelope)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

In light of the amendments, the rejections of Claims 124, 163, 164, and 170-173 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al.

(2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., as applied to Claims 124, 163, and 170-173, further in view of Goncalves, et al. (2001) Virology, 288(2): 236-46, are withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

In light of the amendments, the rejections of Claims 124, 163, 170-173, and 175 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., as applied to Claims 124, 163, and 170-173, above, and further in view of U.S. Patent No. 7,256,036 to Legrand, et al., are withdrawn.

To wit, as shown above, the 102 base reference, Mason, does not teach the feature of encoding the complement-inhibiting sequence.

****** NEW REJECTIONS UTILIZING ART TO DEMONSTRATE USE OF A SINGLE ESSENTIAL PROTEIN IN TRANS******

I. Base Rejection: retroviral vectors with a generic complement inhibitor on its surface and encoded by the genome. This demonstrates the non-allowability of the broad claim as compared to the various species.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 170, 171, and 173 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., and U.S. Patent No. 6,235,522 to Kingsman.

Mason teaches transforming tissues in vivo (e.g., Summary of the Invention), with retroviral vectors with gp70 envelope glycoproteins (e.g., Id., paragraph 3) which are chimerically expressing complement inhibitors (Id.), e.g., those found in pathogens (CIMs) (e.g., BACKGROUND, V. Inhibitors of the Complement System). In addition the vector which is administered is a retroviral vector (Summary of the Invention), and can have the gene encoding the gp41-CIM in the genome and linked to the expression control sequence (e.g., Id., paragraph 1, applicable to new claims 170, 171 (as it targets the complement system), 173 (the specification teaches promoters)). Still further, if enablement is to be questioned, it appears that the claims encompass the same complement inhibitors (e.g., Claims 1 and 8, and definition of "complement inhibitor" in specification, paragraph preceding Section IV., The Complement System), and still further, Claim 13, compared to Claim 14, demonstrates that Claim 13 specifically encompasses in vivo administrations. In addition, the use of a transgene for gene therapy is taught (e.g.,

section "II. Gene Transfer for Gene Therapy"), which inherently requires a transgene connected to a promoter for expression, at least for the protein encoding sequences described in the same section.

However, Mason does not teach that genes of the envelope protein can be encoded by the vector.

On the other hand, it is known that this is done in the process of providing for vectors which are defective, and therefore do not further reproduce once administered and infect more cells. Kingston, however, teaches that such genes can be excluded from the genome (e.g., Brief Summary, paragraph 15), and in doing so recognizes that as long as the vector is defective and incapable of replication, it can encode any particular essential gene, including envelope proteins.

Hence, at the time of invention, it would have been obvious to modify Mason to utilize vectors, including those of Kingston, in performing the invention. The Artisan would do so to provide vectors which provide the same effect, inhibiting complement, while still being defective, and useful in gene therapy, without in vivo replication. The Artisan would also have had a reasonable expectation of success, as the Art is utilized for Art-recognized purposes.

Response to Argument – 103(a), Mason, as now applied with Kington

Applicant has avoided argument to further modification to encode the gene in the genome, as no rejection had yet been proffered, and hence, the rejections as now proffered now require new argument. The argument was simply to Mason alone, without further modification (Argument of 11/18/10, pp. 14-16).

II. Modifications of the Retroviral Base Rejection to Utilize Adenoviral Vectors

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, and 170-173 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., and U.S. Patent No. 6,235,522 to Kingsman as applied to claims 124, 170, 171, and 173 above, and further in view of Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., for reasons of record.

As shown above, Mason and Kinsman make obvious expression of fusion proteins to place a complement inhibitor onto the surface of a retroviral vector and use to transform tissues. However, Mason and Kingsman do not make teach or make obvious the use of adenoviral vectors.

On the other hand, it is well known that adenoviral vectors suffer from complement-mediated inactivation (e.g., Xing, et al. (2001) Cell Research, 11(2): 116-24, figure 5B). Moreover, it is well known to link peptides to be displaced on the surface of an adenovirus (e.g., U.S. Patent No. 7,468,181 to Vogels, et al., paragraph 6 of the Detailed Description, describing the addition of peptides to several surface displayed proteins of adenoviruses).

Further, it is well known that adenoviral vectors contain other targeting motifs, e.g., in the knob, fiber, and penton bases. Moreover, Vogels teaches that Serotype 5 is common serotype of adenovirus which is utilized for transformations (e.g., Detailed description), and it

contains an RGD motif. (For the sake of clarity, it is also Officially Noted that Adenovirus Type 5 is well known for gene therapy protocols.)

Hence, it would be obvious to modify the Mason to utilize adenoviral vectors. The Artisan would do so to provide adenoviral vectors for administration and avoid complement-mediated inactivation. Moreover, the Artisan would have had a reasonable expectation of success, as it was already to so-display peptides, and Adenoviruses are well known for gene delivery.

Response to Argument – 103(a), Mason (and now Kingsman), Xing, Vogels

Applicant's argument is limited to the missing teaching to encode the complement-inhibiting protein within the genome of the vector (pp. 17-18)

Such is no longer applicable, as Kingsman is now present.

III. Modification of (II) to Utilize a Hypervariable Region

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, and 170-173 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., U.S. Patent No. 6,235,522 to Kingsman, Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., as

applied to claims 124, 163, and 170-173 above, and further in view of U.S. Patent No. 6,127,525 to Crystal, et al., for reasons of record.

As shown above, the various references make obvious the claims, except the aspect of utilizing a hypervariable region for inserting the peptide.

Crystal demonstrates that several hypervariable regions of adenovirus may be deleted and/or substituted with chimeric peptides (e.g., paragraphs 11-12 of the section titled "Chimeric Adenovirus Coat Proteins").

As such the Artisan would find the invention obvious over the art. The Artisan would modify the references as Crystal demonstrates that these regions are tolerant to changes and it would place the peptide on the surface of the virus. Moreover, the Artisan would have a reasonable expectation of success, as Crystal teaches it would work, and Mason teaches that the peptides would work to ameliorate the complement inactivation of the virus.

Response to Argument – 103, in view of crystal

Applicant's argument of 11/18/10 has been fully considered but is not found persuasive.

Applicant's argument is limited to the missing teaching to encode the complement-inhibiting protein within the genome of the vector (pp. 17-18)

Such is no longer applicable, as Kingsman is now present.

IV. Modification of (II) or (III) to utilize ED1

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, and 169-173 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., U.S. Patent No. 6,235,522 to Kingsman, Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al as applied to claims 124, 163, and 170-173 above (II), and further in view of Inal, et al. (2000) FEBS Letters, 470: 131-34; and

Claims 124, 163, and 169-173 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., U.S. Patent No. 6,235,522 to Kingsman, Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., and U.S. Patent No. 6,127,525 to Crystal, et al., as applied to claims 124, 163, and 170-173 above (III), and further in view of Inal, et al. (2000) FEBS Letters, 470: 131-34.

As shown above, the various references make obvious the invention in each case, except that the references do not teach or make obvious the ED1 domain.

On the other hand, Inal teaches that the ED1 domain of Sh-TOR inhibits complement and does so when isolated from the normal protein (e.g., ABSTRACT).

Hence, it would be obvious to modify the references to arrive at the invention. The Artisan would do so to inhibit complement inactivation of the virus. Moreover, the Artisan

would have a reasonable expectation of success, as Inal has shown that the peptide works out of context.

Response to Argument – 103, references in view of Inal

Applicant's argument of 11/18/10 has been fully considered but is not found persuasive.

Applicant's argument is limited to the missing teaching to encode the complement-inhibiting protein within the genome of the vector (pp. 18-19)

Such is no longer applicable, as Kingsman is now present.

V. Modification of (IV) to Further Include a His-Tag

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, 167, and 169-174 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., U.S. Patent No. 6,235,522 to Kingsman, Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., and Inal, et al. (2000) FEBS Letters, 470: 131-34 as applied to claims 124, 163, and 169-173 above (II), and further in view of Huang, et al. (2000) Protein Expression and Purification, 18: 169-74; and

Claims 124, 163, 167, and 169-174 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., U.S. Patent No. 6,235,522 to

Kingsman, Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., U.S. Patent No. 6,127,525 to Crystal, et al., and Inal, et al. (2000) FEBS Letters, 470: 131-34 as applied to claims 124, 163, and 169-173, and further in view of Huang, et al. (2000) Protein Expression and Purification, 18: 169-74.

As shown above, the various limitations are obviated, except that of utilizing a His-Tag.

However, it was well known in the Art that His-Tagged entities can be isolated utilizing the His-Tag (e.g., Huang, ABSTRACT). Such His-Tag can also be considered as encoded by a reporter NA, as it can be used to report the presence of the protein to which it is attached.

Hence, it would have been obvious to modify the invention to include a His-Tag. The Artisan would do so to provide for easier isolation of the viruses with such ED1 expressed on its surface. Moreover, the Artisan would have a reasonable expectation of success, as it was well known to use His-Tags to isolate entities with such His-Tag.

Response to Argument - 103(a), further in view of Huang

Applicant's argument of 11/18/10 has been fully considered but is not found persuasive.

Applicant's argument is limited to the missing teaching to encode the complement-inhibiting protein within the genome of the vector (pp. 19-20)

Such is no longer applicable, as Kingsman is now present.

VI. Modification of V to Utilize 2 ED1 Sequences and a Linker

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

It is noted that the following rejections rely upon Oh, et al., which is a reference under 102(a), and hence, may be sworn behind to overcome the rejection.

Claims 124, 163, 166, 167, and 169-174 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., U.S. Patent No. 6,235,522 to Kingsman, Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., Inal, et al. (2000) FEBS Letters, 470: 131-34, and Huang, et al. (2000) Protein Expression and Purification, 18: 169-74 as applied to claims 124124, 163, 167, and 169-174 above, and further in view of Oh, et al., (2003) Immunology, 110: 73-79; and

Claims 124, 163, 166, 167, and 169-174 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., U.S. Patent No. 6,235,522 to Kingsman, Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., U.S. Patent No. 6,127,525 to Crystal, et al., Inal, et al. (2000) FEBS Letters, 470: 131-34, and Huang, et al. (2000) Protein Expression and Purification, 18: 169-74 as applied to claims 124, 163, 167, and 169-174, and further in view of Oh, et al., (2003) Immunology, 110: 73-79.

As shown above, the various limitations are obviated, except the use of 2 ED1 sequences, linked by a linker.

On the other hand, Oh teaches that a duplicated ED1 domain provides increased inhibition of complement activation over that of a single ED1 domain (p. 76, col. 2, paragraph 2). In addition, the linker may be as little as a peptide bond, given the broadest reasonable

interpretation, and also, Oh teaches that amino acid 27 is not important, but is necessarily present in their homodimer (p. 78, paragraph 1).

Hence, it would have been obvious to modify the references to utilize Oh's ED1 duplicated domain. The Artisan would do so to increase complement inhibition. Moreover, the Aritsan would expect success, as Oh teaches that complement inactivation is greater than single ED1 domains.

Response to Argument – 103(a) further in view of Oh

Applicant's argument of 11/18/10 has been fully considered but is not found persuasive.

Applicant's argument is limited to the missing teaching to encode the complement-inhibiting protein within the genome of the vector (p. 20).

Such is no longer applicable, as Kingsman is now present.

VI. Modification of (II) to Utilize an AAV vector (AAV vector in AdV envelope)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, 164, and 170-173 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., U.S. Patent No. 6,235,522 to

Kingsman, Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., as applied to Claims 124, 163, and 170-173, further in view of Goncalves, et al. (2001) Virology, 288(2): 236-46.

The rejection is maintained because there is no art for the Examiner to determine that an AAV genome, within an AdV envelope should not be, given its broadest reasonable interpretation, considered an AAV vector.

As shown above, the references obviate the claims, except the use of an AAV vector.

Goncalves, however, teaches encapsulation of AAV vectors into Adenoviral envelopes, to thereby allow superior prolonged transgene expression and allowing larger inserts (e.g., ABSTRACT). Moreover, the transgenes for packaging from adenovirus are entered into the AAV genome (e.g., ABSTRACT).

Hence, it would have been obvious to make the invention as claimed. The Artisan would do so to increase the the time of transgene expression and allow larger inserts than AAV enveloped AAV vectors. Moreover, the Artisan would expect success, as Goncalves teaches it can be done.

Response to Argument – 103(a), further in view of Goncalves

Applicant's argument of 11/18/10 has been fully considered but is not found persuasive.

Applicant's argument is limited to the missing teaching to encode the complement-inhibiting protein within the genome of the vector (p. 21).

Such is no longer applicable, as Kingsman is now present.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, 170-173, and 175 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., U.S. Patent No. 6,235,522 to Kingsman, Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., as applied to Claims 124, 163, and 170-173, above, and further in view of U.S. Patent No. 7,256,036 to Legrand, et al.

As shown above, the various aspects of the claims are obvious, except for the presence of a mutation in a CAR binding site.

On the other hand, Legrand teaches adenoviral vectors for use in gene therapy, which are modified in their CAR binding sites (e.g., Claim 1, "abolishing the capacity of said adenovirus for binding to the natural cellular receptor"; Brief Summary, paragraph 25, indicating that the natural cellular receptors encompass the receptor for CAR; and the concluding paragraph indicating that insertion of new ligands can redirect affinity to other cell types). Further mutation of the penton base can remove binding to integrins (e.g., paragraph 9 of the Breif summary). Doing so can remove normal tropism, allow the Artisan to modify the tropism with new targeting ligands (e.g., Id.).

Hence, it would be obvious to modify the CAR binding region or remove the integrin-biding region. The Artisan would do so to redirect targeting to distinct cell types and remove natural targeting. Moreover, the Artisan would expect success, as Legrand teaches such.

Response to Argument – Mason/Kingsman/Xing/Vogels/Legrand

Applicant's argument of 11/18/10 has been fully considered but is not found persuasive.

Applicant's argument is limited to the missing teaching to encode the complement-inhibiting protein within the genome of the vector (pp. 21-22).

Such is no longer applicable, as Kingsman is now present.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Primary Examiner, Art Unit 1633